NTNU

Faculty of Medicine
Department of Laboratory Medicine, Children's and Women's Health

Exam MOL3001
Medical genetics

Friday 31 May 2013, 9.00 am - 1.00 pm

ECTS credits: 7.5
Number of pages (including front-page): 3
Examination support: Calculator and English dictionary

Contact person during the exam: Wenche Sjursen (72573530; 93666916)

Exam results: June 21th 2013
Examination results are announced on http://studweb.ntnu.no/

All questions are equally rated (25% for each of question 1-4). The subquestions are not equally rated (these are marked)

Examination question 1.

Emma, 45 years old, was diagnosed with hypercholesterolemia after a myocardial infarction. Her father died only 40 years old of myocardial infarction, whereas her mother (65 years old) is still alive and healthy. Emma is married to Henrik who has no known heart condition. Testing of the cholesterol level in their two children, a girl and a boy, showed that their son is also affected. Emma's younger sister has a son with her present husband and two daughters from a previous marriage. Their cholesterol levels were within normal ranges. Emma's older sister has received treatment for hypercholesterolemia for many years. She has two sons, one of which has hypercholesterolemia. The affected son has three daughters, of whom one is affected.

The family history indicates familial hypercholesterolemia. However, no mutations were found in genes known to cause hypercholesterolemia. A linkage analysis identified a linkage region and the genotypes of three markers in the 1st and 2nd generation of the family are:

	Emma's mother	Older sister	Emma	Younger sister
Marker 1	201 201	201 215	201 215	201 215
Marker 2	192 192	192 198	192 198	192 188
Marker 3	244 244	244 260	244 260	244 250

a) Draw the pedigree and mark out the genotypes shown in the table. (20%)

b) What is the possible mode of inheritance? Explanation your answer. (20%)

c) What type of markers is used in the linkage analysis, SNPs, microsatellites, minisatellites or copy number variants? Explain your answer and describe why they are especially useful for genetic linkage analysis. (30%)

d) Deduce the genotypes of Emma's father. The genotypes in the table are phased. What is a haplotype, why is it important to know the phase, and which haplotype seems to be linked to the disease? How could one decide if a marker in a linkage study is linked to an unknown disease gene? (30%)

Examination question 2.

a) Cytogenetic is the study of the structure and function of the cell and especially the chromosomes. Describe the most common numerical chromosomal aberrations and explain how they arise. (30%)

b) Describe shortly different methods used to discover chromosomal disorders. (30%)

c) Cystic fibrosis is a hereditary disorder with autosomal recessive inheritance pattern affecting approximately 1 in 2500 newborn in Europe. Based on the Hardy Weinberg Equilibrium, calculate the: (40%)

1) Frequency of the recessive allele in the population.
2) The frequency of the dominant allele in the population.
3) The percentage of heterozygous carriers in the population.

Examination question 3.

Concordance and Discordance are concepts often used to describe the co-occurrence or not co-occurence of the same disease in pairs of relatives (e.g. in twins).

a) Describe in principal terms the expected observation with regard to concordance and discordance rates in monozygotic twins and same-sex dizygotic twins for 1) a disease with a significant genetic component, and 2) a disease with little or no genetic influence. (30%)

b) In a given monzygotic twin pair, only one of the two twins is affected with a multifactorial disease known to have a strong genetic component. What are possible explanations for the observation? (20%)

c) If you expect a disease or trait to be primarily influenced by the environment, and not by genetics, which twin-study design(s) would you chose in order to test your hypothesis? Explain your choice. (20%)

d) Twin studies are useful when trying to quantify the relative contribution of genes and environment to a multifactorial disease, but such studies also have several limitations. List some of the possible limitations of twin studies. (30%)

Examination question 4.

a) A genetic disease occurs when an alteration in the DNA of an essential gene changes the amount or function, or both, of the gene products – most commonly proteins. Single gene disorders almost always result from mutations that affect a protein. Effects on protein include:

1) Loss-of-function
2) Gain-of-function
3) Novel property

Explain the terms 1-3. Place the following diseases to the correct effects mentioned above: Sickle cell disease and the most common forms of α-thalassemia. (40%)

b) Describe what is meant by mosaicism. (30%)

c) The Act relating to the application of biotechnology in human medicine (Biotechnology Act); regulates the use of biotechnology in Norway. What is the purpose of the Act?
§ 5 is about postnatal testing and distinguishes between the different purposes of testing, predictive and diagnostic. What is the main difference and how are they treated differently? (30%)

Made by Linda Tømmerdal Roten, Frank Skorpen, Inga Bjørnevoll and Wenche Sjursen